REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claim Amendment

Claims 1-4, 7-8, 11-13, 16-17, and 20-21 are pending in this application.

Claims 5-6, 9-10, 14-15, 18-19, and 22-27 stand cancelled.

Claim 1 is currently being amended to recite the phrase, "5,6-dimethylxanthenone-4-acetic acid," which is a full meaning of the term "DMXAA." No new matter is added by this amendment. Support for this amendment can be found, for example, on page 1 of the application as filed.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, Claims 1-4, 7-8, 11-13, 16-17, and 20-21 are pending in this application and are under consideration.

Priority

Applicants thank the Office for acknowledging Applicants' claim for foreign priority based on GB application filed on 9/3/2001. The Office, however, has granted the earliest effective date of the instant application for prior art purposes to be September 3, 2002 which is the filing date of the PCT/GB02/04025. The Office has requested the Applicant to provide a certified copy of the GB0121285.1. *See* page 3, ¶1 and 2 of the Office Action.

Applicants concurrently herewith provide a certified copy of the GB0121285.1 by express mail. The Office is requested to acknowledge the earliest effective date of the instant application to be September 03, 2001.

Information Disclosure Statement

Applicants thank the Office for acknowledging and considering the IDS filed on 10/31/2007.

Claim Rejection under 35 U.S.C. §112, second paragraph

Claims 1-4, 7-8, 11-13, 16-17, and 20-21 are rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office alleges that Claim 1 recites the abbreviation "DMXAA" and that the first use of the abbreviation in the claims should be preceded by the full meaning of the abbreviation. *See* page 3, last paragraph to page 4, firs paragraph.

Applicants have amended Claim 1 to recite the full meaning of the term "DMXAA." Withdrawal of this rejection is respectfully requested.

Claim Rejections under 35 U.S.C. §103(a)

A. Claims 1-4, 7-8, 11-13, 16-17, and 20-21 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Davis (WO 00/48591; Published 8/24/2000) in view of Applicants' disclosure at page 9, line 14 and page 12, lines 17-19. The Office alleges that Davis teaches methods of inhibiting the formation of new vasculature by angiogenesis by administering a combination of a vasculature damaging agent and an inhibitor of the formation or action of nitric oxide in further combination with other anti-tumor agents such as 5-fluorouracil. The Office further alleges that one skilled in the art would have been imbued with at least a reasonable

expectation that a combination of DMXAA, a nitric oxide inhibitor, and gemcitabine would be an effective treatment for solid tumors. *See* pages 4-7 of the Office Action.

Applicants traverse the rejection for the following reasons:

> To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Davis does not teach or suggest all the claim limitations

Davis does not teach or suggest all the claim limitations. The instant claims are directed to treatment of solid cancerous tumor using a combination of 5,6-dimethylxanthenone-4-acetic acid (DMXAA) or a pharmaceutically acceptable salt thereof and gemcitabine. Davis does not teach or suggest gemcitabine in combination with DMXAA as in instant claims. At best, Davis discloses 5-fluorouracil as an example of an antimetabolite to be used in combination with vasculature damaging agent and an inhibitor of the formation or action of nitric oxide (*see* Davis, page 6, lines 25-26).

The Office has combined Davis with the instant application and has alleged that, "Applicants acknowledge that gemcitabine and 5-fluorouracil are suitable antimetabolites of use in combination with DMXAA, thus teaching their functional equivalence." *See* page 6, ¶1 of the Office Action).

The Office's position, at best, appears not to be based on the teachings of the references as whole, but to be based on the knowledge learned from the Applicants' disclosure which cannot support a finding of obviousness. *See In re Dow Chem. Co. v. American Cyanamid Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988) ("[t]here must be a reason or suggestion in the art for

selecting the procedure used, other than the knowledge learned from the applicant's disclosure."). The motivation to combine the references cannot come from the teachings of the specification itself. *In re Lee*, 277 F.3d 1338, 1343, *citing W.L. Gore v. Garlock, Inc.* 721 F.2d 1540, 1553 (Fed. Cir. 1983) (it is improper to use that which the inventor taught against its teacher). Evidence that the Office has supported the basis for the combination of Horie with the secondary references is found on page 21 of the Office Action which points to Applicants' specification for support to apply the Office's interpretation of Horie to the secondary references: "[Applicants'] specification states "Patients with triple repeat in the TS gene as expected from in vitro models had higher gene expression levels..." (emphasis in Office Action). This statement relates to the Applicants' own work and therefore it cannot be used against the Applicants as prior art or in framing a rejection under 35 U.S.C. § 103. *See Reading & Bates Constr. Co. v. Baker Energy Resources Corp.*, 748 F.2d 645 (Fed. Cir. 1984).

Further, Applicants contend that the instant application discloses gemcitabine as a nucleotide analogue antimetabolite and 5-fluorouracil as antineoplastic antimetabolite as anti-cancer agents (*see* page 12, lines 17-19 and page 13, lines 1-2 of the instant application). The instant application makes no admission of their functional equivalence let alone any admission of replacing one with the other.

The instant application shows that the anticancer agents belonging to the same class are not necessarily active anti-cancer agents. For example, the instant application discloses both carboplatin and cisplatin as platinum chemotherapeutic agents (*see* page 12, lines 12-16 of the instant application). However, Example 1 of the instant application in the results section (*see* page 28, lines 19-25 of the instant application) shows that even though cisplatin as a single agent showed appreciable activity, carboplatin as a single agent was essentially inactive anti-cancer agent. This further corroborates the fact that one anti-cancer agent may not be replaced with another anti-cancer agent by virtue of them being in the same class. Additionally, Example 1 of the instant application shows that the synergistic interaction of DMXAA with other anti-cancer agents tested was significantly greater than unity for all drugs (quantified as DMF) except 5-

fluorouracil (*see* page 30, lines 7-8 of the instant application). Therefore, the Office's assertion that gemcitabine and 5-fluorouracil are functionally equivalent, is in error.

Hence, Davis does not teach or suggest all the claim limitations.

No suggestion or motivation to modify the reference

Davis discloses a long list of anticancer agents (*see* Davis, page 6, lines 20-30) that can be used in combination with DMXAA and an inhibitor of the formation or action of nitric oxide. Davis provides no suggestion or motivation to a person of ordinary skill in the art to pick and choose an antimetabolite, such as 5-fluorouracil, from that list and further replace it with another antimetabolite, gemcitabine, to arrive at the claimed invention.

The instant application shows that DMXAA in combination with other anti-cancer agents demonstrates synergistic anti-tumor activity (*see* page 25, Example 1 of instant application). Example 1 of the instant application demonstrates that co-administration of DMXAA with other anti-cancer agents produced a large enhancement of tumor growth delay (*see* for example, page 29, lines 5-13 of instant application). This is in contrast to Davis where even though Davis states that the efficacy of vascular damaging agents can be improved by combining the treatment with inhibitors of the formation or action of nitric oxide (*see* Davis, page 2, lines 7-9), it discloses no such synergistic correlation of the vascular damaging agents and the inhibitors of nitric oxide with other anti-tumor substances such as, 5-fluorouracil. Therefore, a person of ordinary skill in the art cannot envisage such synergy between DMXAA and 5-fluorouracil and further replace 5-fluorouracil with gemcitabine to come up with the claimed invention.

Hence, in the absence of any suggestion or motivation in Davis, a person of ordinary skill in the art cannot arrive at the claimed invention.

No reasonable expectation of success

There is no reasonable expectation of success to a person of ordinary skill in the art to pick and choose 5-fluorouracil and further replace it with gemcitabine to arrive at the claimed

invention. As explained *supra*, one anti-cancer agent may not be replaced with another anti-cancer agent by virtue of them being in the same class. Additionally, Example 1 of the instant application also shows that each active anti-cancer agent may possess a different synergistic activity. Example 1 of the instant application shows that the magnitude of the synergistic activity between the active anti-cancer agents may also differ (*see* page 29, lines 5-13 of the instant application). Therefore, there is no reasonable expectation of success to a person of ordinary skill in the art to pick 5-fluorouracil from Davis, replace it with gemcitabine and expect it to be not just active but also have a synergistic anti-tumor activity with DMXAA.

In light of the arguments as provided *supra*, withdrawal of this rejection under 35 U.S.C. §103(a) as being unpatentable over Davis, is respectfully requested.

B. Claims 1-4, 7-8, 11-13, 16-17, and 20-21 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Siemann *et al.* (Proceeds of the American Associate for Cancer Research, 2000, vol. 41, Page 525) and Pruijn *et al.* (Cancer Chemother. Pharmacol., 1997, col. 39, pages 541-546) in view of Grindley *et al.* (USP No. 5,464,826; Issued Nov. 7, 1995) (newly cited) and van Moorsel *et al.* (Biochemical Pharmacology, 1997, vol. 57, pages 407-415).

The Office alleges the following:

Siemann *et al.* demonstrates that DMXAA potentiates the antitumor effect of two traditional chemotherapeutic agents, namely, cisplatin and cyclophosphamide, in a mammalian tumor model of breast and ovarian tumors (*see* page 8, ¶1 of the Office Action). Pruijn *et al.* teach enhancing the antitumor activity of an anticancer agent, melphalan with DMXAA. Prujin *et al.* motivates one skilled in the art to formulate the compositions recited in instant claims 7-8, 11-13, 16-17, and 20-21. Prujin *et al.* expressly suggest concomitant and sequential administration as recited in claims 3-4. *See* page 8, ¶1 of the Office Action. Grindley *et al.* provide that gemcitabine is known to be effective in treating cancer. *See* page 9, ¶3 of the Office Action. Van Moorsel *et al.* disclose combination chemotherapy studies with gemcitabine and

etoposide in non-small cell lung and ovarian cancer cell lines. *See* page 9, ¶4 to page 10, ¶1 of the Office Action.

Further, the Office cites *In re Kerkoven*, 205 USPQ 1069 (CCPA 1980) and *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). *See* pages 10-12 of the Office Action.

Applicants traverse the rejection for the following reasons:

The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) reviewed the analysis for determining if an invention is obvious over the teachings of the prior art and affirmed the factual analysis set forth in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966). *KSR*, 127 S. Ct. at 1734 (quoting *Graham*, 383 U.S. at 17-18). The factual inquiries necessary in an analysis of obviousness by the Office is delineated in MPEP § 2141 as follows:

(A) Determining the scope and contents of the prior art;

(B) Ascertaining the differences between the prior art and the claims in issue;

(C) Resolving the level of ordinary skill in the pertinent art; and

(D) Evaluating evidence of secondary considerations...

MPEP § 2141 further states that:

When applying 35 U.S.C. 103...

(A) The claimed invention must be considered as a whole;

(B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;

(C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and

(D) Reasonable expectation of success is the standard with which obviousness is determined.

Application of the obviousness analysis of KSR, *supra*, was discussed in the recent decision by the Court of Appeals for the Federal Circuit in *Takeda Chemical Industries Ltd. v. Alphapharm Pty. Ltd.*, 83 U.S.P.Q.2d 1169, page 7, left column, ¶1 (Fed. Cir. 2007). The CAFC held that:

> "[w]hile the KSR Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test in an obviousness inquiry, the Court acknowledged the importance of identifying "a reason that would have prompted a person skilled in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. KSR, 127 S. Ct. at 1731. Moreover, the Court indicated that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis". *Id.* As long as the test is not applied as a "rigid and mandatory" formula, that test can provide "helpful insight" to an obviousness inquiry. *Id.*"

Applicants' herein would apply the claimed invention consistent with Graham analysis and the ruling in *KSR*, and will show that Applicants' claimed invention meets the criteria of 35 U.S.C. §103.

(A) The Scope and Content of the Prior Art

Siemann *et al.* teach combination of DMXAA with cisplatin or cyclophosphamide examined in the rodent and human tumor models. Siemann *et al.* do not teach gemcitabine. Further, Siemann *et al.* do not teach gemcitabine in combination with DMXAA, as in the claimed invention.

Pruijn *et al.* teach enhancing the antitumor activity of an anticancer agent, melphalan with DMXAA. Pruijn *et al.* do not teach gemcitabine. Further, Pruijn *et al.* do not teach gemcitabine in combination with DMXAA ,as in the claimed invention.

Grindley *et al.* teach treating neoplasms using gemcitabine. Grindley *et al.* do not teach gemcitabine in combination with another anti-cancer agent. In particular, Grindley *et al.* do not teach gemcitabine in combination with DMXAA, as in the claimed invention.

Van Moorsel *et al.* teach combination chemotherapy studies with gemcitabine and etoposide in ovarian cancer cell lines. Van Moorsel *et al.* do not teach gemcitabine in combination with DMXAA, as in the claimed invention.

(B) The Differences Between The Cited Art and The Claimed Invention

The claimed invention is directed to a method for treating a solid cancerous tumor, which comprises administering to a mammal in need of such treatment an effective amount of 5,6-dimethylxanthenone-4-acetic acid (DMXAA) or a pharmaceutically acceptable salt thereof and administering an effective amount of gemcitabine.[1] Applicants' invention is based on the result that the administration of gemcitabine in combination with DMXAA demonstrates synergistic anti-tumor activity (*see* page 32, Example 2 of instant application).

Siemann *et al.* teach combination of DMXAA with cisplatin or cyclophosphamide. Neither Siemann *et al.* teach gemcitabine nor Siemann *et al.* teach gemcitabine in combination with DMXAA. Siemann *et al.* do not suggest or motivate a person of ordinary skill in the art to pick gemcitabine from all the anti-cancer agents known in the art and use it in combination with DMXAA, as in the claimed invention. Mere recitation of cisplatin or cyclophophamide in combination therapy with DMXAA, as in Siemann *et al.*, is not a suggestion or motivation to pick gemcitabine in the combination therapy. As explained *supra*, Example 1 of the instant application demonstrates that each active anti-cancer agent may possess a different synergistic activity with DMXAA. Example 1 of the instant application also demonstrates that the magnitude of the synergistic activity between the active anti-cancer agents may also differ (*see* page 29, lines 5-13 of the instant application). Therefore, in the absence of a suggestion or motivation in Siemann *et al.*, a person of ordinary skill in the art will have no reasonable expectation of success to choose gemcitabine from a plethora of anti-cancer agents known in the art and use it in a combination with DMXAA.

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[1] This brief summary is provided for illustrative purposes only and is not to be construed as limiting, modifying or altering the scope of each of the independent claims provided. The Examiner is requested to review the independent claims to determine the exact scope of the claimed invention.

Pruijn *et al.* teach co-administering melphalan with DMXAA. Like Siemann *et al.*, Pruijn *et al.* too merely teach a combination of DMXAA with another anti-cancer agent and do not teach gemcitabine in combination with DMXAA. There is no suggestion or motivation in Pruijn *et al.* to pick gemcitabine from all the anti-cancer agents known in the art and use it in combination with DMXAA, as in the claimed invention. In the absence of any suggestion or motivation, there is no reasonable expectation of success to a person of ordinary skill in the art to pick and choose gemcitabine from a plethora of anti-cancer agents known in the art and use it in combination with DMXAA.

Grindley *et al.* teach treating neoplasms using gemcitabine. Grindley *et al.* do not teach gemcitabine in combination with any other anti-cancer agent. In particular, Grindley *et al.* do not teach gemcitabine in combination with DMXAA, as in the claimed invention. Applicants do not dispute the Office's assertion that gemcitabine is a compound known to be effective in treating cancer. However, Grindley *et al.* do not suggest or motivate a person of ordinary skill in the art to use gemcitabine in combination with other anti-cancer agents let alone DMXAA.

Finally, van Moorsel fails to fulfill the gap left out by Siemann etal., Pruijn *et al.*, and Grindley *et al.* Van Moorsel *et al.* merely teach combination of gemcitabine with etoposide in ovarian cancer cell lines. Van Moorsel *et al.* do not teach gemcitabine in combination with DMXAA, as in the claimed invention. Van Moorsel *et al.* do not suggest or motivate a person of ordinary skill in the art to use gemcitabine in synergistic combination with DMXAA.

Therefore, neither of the cited references alone or in combination suggest or motivate a person of ordinary skill in the art to arrive at the claimed invention.

The Office alleges that in the absence of a showing of unexpected results commensurate in scope with the claims, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to administer DMXAA in combination with gemcitabine as taught by Siemann, *et al.* and Pruijn, *et al.* in view of Grindley *et al.*, and van Moorsel, *et al.* *See* page 10, ¶2 of the Office Action. The

Office further alleges that, "[o]ne of ordinary skill in the art would have been imbued with at least a reasonable expectation that gemcitabine and DMXAA in combination would be effective in treating solid tumors." *See* page 10, ¶2 of the Office Action.

Supreme Court in *KSR* noted that exemplary rationales that may support a conclusion of obviousness include:

> (A) Combining prior art elements according to known methods to yield predictable results;
>
> (B) Simple substitution of one known element for another to obtain predictable results;
>
> (C) Use of known technique to improve similar devices (methods, or products) in the same way;
>
> (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;
>
> (E) "Obvious to try" - choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;
>
> (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;
>
> (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

Synergistic combination of two anti-cancer drugs, such as, DMXAA and gemcitabine, is not a predictable field. As is shown *supra*, two anti-cancer agents may not just differ in their anti-tumor activity but may also differ in their synergistic activity and a magnitude of synergism. In the absence of any teaching, suggestion or motivation in any of the cited references, a person of ordinary skill in the art cannot choose gemcitabine from a plethora of anti-cancer agents known in the art and combine it with DMXAA to arrive at the claimed invention. There is no reasonable expectation of success to pick gemcitabine in combination with DMXAA since each anti-cancer agent may demonstrate a different synergistic activity.

Applicants assert that the Office has resorted to impermissible hindsight.

> The requirement "at the time the invention was made" is to avoid impermissible hindsight. "It is difficult but necessary that the decision maker forget what he or she has been taught . . . about the claimed invention and cast the mind back to the time the invention was made (often as here many years), to occupy the mind of one skilled in the **art. >...<" *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303, 313 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

Applicants submit that the Office has resorted to impermissible hindsight as the Office has cited different arts to put together the elements of the claimed invention where none of the cited art individually or in combination teach, suggest or motivate a person of ordinary skill in the art with any reasonable expectation of success to arrive at the claimed invention.

The Office has cited *In re Kerkoven*, 205 USPQ 1069 (CCPA 1980) and *In re Sernaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). *See* pages 10-12 of the Office Action.

The Office alleges that in *In re Kerkoven*, the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose. The Office further alleges that while *In re Kerkoven* is limited to the mechanical arts, the holdings in this case are pertinent to the present claims because the idea of combining two known anticancer drugs to treat cancer flows logically from the individual drugs being taught to be useful in treating cancer.

In *In re Kerkoven*, the Appellant's invention covers two separate methods of producing mixed-active particulate detergents, each method including the common step of forming at least two slurries [FN3] of detergent ingredients, the active detergent content of one slurry being primarily if not exclusively anionic in nature and the active ingredient content of the other slurry being primarily if not exclusively nonionic in nature. Under these methods, the slurries are independently dried and the resulting products are mixed or the slurries are simultaneously dried and then mixed.

Applicants submit that a rationale for citing *In re Kerkoven* in the instant application is baseless. Firstly, the predictability in the field of mixing detergents is much higher than the

predictability of using different drugs in the field of cancer treatment. The behavior of an anti-cancer drug or a combination of anti-cancer drugs in the human body is much more complex than mixing of the ingredients of the detergent to create a detergent of particular properties. As shown *supra*, the determination of obviousness would differ based on the predictability in the field. Secondly, Coffey, the prior art cited by the Office in *In re Kerkoven*, clearly discloses using all the ingredients to prepare a slurry. Coffey differs from the Appellant in mixing the ingredients in one slurry which is then spray dried. Therefore, there is at least one reference, namely, Coffey, which provides all the ingredients needed for the slurry. This is in sharp contrast to the instant application where none of the references cited by the Examiner teach or suggest the components of the claimed invention, namely, a combination of gemcitabine and DMXAA. Siemann *et al.* and Pruijn *et al.* do not even mention gemcitabine. Grindley *et al.* and Pruijn *et al.* only disclose gemcitabine or gemcitabine in combination with etoposide. There is no suggestion or motivation to a person of ordinary skill in the art to combine the references and come up with the claimed invention.

Hence, *In re Kerkoven* does not apply to the claimed invention.

The Office cites *In re Sernaker* and alleges that the rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination.

The Appellants' invention in *In re Sernaker* relates to a type of embroidered emblem. Firstly, the predictability in the field of embroidered emblem is much higher than the predictability of using different drugs in the field of cancer treatment. The behavior of an anti-cancer drug or a combination of anti-cancer drugs in the human body is much more complex than creating an embroidered emblem. As shown *supra*, the determination of obviousness would differ based on the predictability in the field.

Secondly, In *In re Sernaker*, the court stated that the question to be answered in correctly deducing obviousness,from the prior art are that a) whether a combination of the teachings of all or any of the references would have suggested (expressly or by implication) the possibility of achieving further improvement by combining such teachings along the line of the invention in suit, and b) whether the claimed invention achieved more than a combination which any or all of the prior art references suggested, expressly or by reasonable implication.

None of the references cited by the Office suggest (expressly or by implication) the combination of gemcitabine with DMXAA. Siemann *et al.* and Pruijn *et al.* do not even mention gemcitabine. Grindley *et al.* teach gemcitabine for treating neoplasms and do not suggest a combination of gemcitabine with any other drug let alone DMXAA. Lastly, van Moorsel *et al.* teach gemcitabine in combination with etoposide and do not teach gemcitabine combination with any other agent.

Hence, *In re Sernaker* also does not apply to the claimed invention.

(C) Evaluating evidence of secondary considerations

Assuming *arguendo*, that the Office has established a *prima facie* case of obviousness, the instant application shows surprising results that DMXAA in combination with gemcitabine demonstrates anti-tumor activity much higher than the anti-tumor activity of each of gemcitabine or DMXAA alone (*see* page 32, Example 2 of the instant application). Such results rebut any such *prima facie* case.

In light of the arguments as presented above, Applicants request the Office to withdraw this rejection based on 35 U.S.C. §103(a).

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

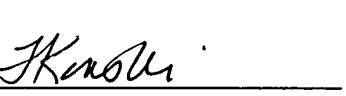
CONCLUSION

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date August 20, 2008

By 

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